Inorganica Chimica Acta, *106* (1985) 177–180

X-ray Structure of a Mono(1-Methylthyminato) Complex of Cisplatin, Chloro-(1-methylthyminato-*N3*)-*cis*-diammineplatinum(II) Monohydrate

HELMUT SCHÖLLHORN, ULF THEWALT*

Sektion für Röntgen- und Elektronenbeugung, Universität Ulm, D-79 Ulm, F.R.G.

and BERNHARD LIPPERT*

Anorganisch-Chemisches Institut, Technische Universität München, D-8046 Garching, F.R.G.

Received September 13, 1984

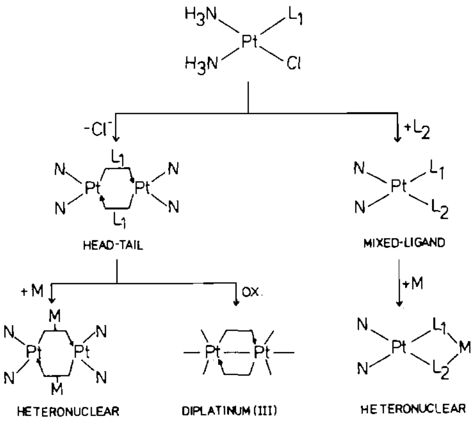
Abstract

The crystal structure of chloro-(1-methyltyminato-*N3*)-*cis*-diammineplatinum(II) monohydrate, *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)Cl \cdot H_2O$, is reported. The compound crystallizes in space group $P\bar{1}$ with a = 6.911(2) Å, b = 8.598(3) Å, c = 11.464(4) Å, α = 100.13(3)°, β = 120.03(3)°, γ = 93.16(3)°, Z = 2. The structure was refined to R = 0.048 and R_w = 0.057. The compound contains the deprotonated 1-methylthymine ligand coordinated to Pt through N3 (1.973(10) Å). This distance represents the shortest Pt-N3(pyrimidine-2.4-dione) bond reported so far. The two Pt–NH_3 bond lengths differ significantly: Pt–NH_3 (*trans* to Cl) is longer (2.052(10) Å) than Pt–NH_3 (*trans* to N3 of 1-MeT) (2.002(11) Å). The Pt–Cl distance (2.326(3) Å) is normal, as is the large dihedral angle between the Pt coordination plane and the nucleobase (76.5°).

Introduction

Mono(nucleobase) complexes of *cis*-$(NH_3)_2Pt(II)$ are convenient starting materials for dinuclear (head–tail) complexes [1], mixed-nucleobase complexes [2–4], and heteronuclear derivatives of these compounds [5], as well as for novel diplatinum(III) complexes [6] (scheme 1). Complexes of these types are of interest with regard to metal–metal interactions within di- or oligonuclear species and also as models of possible DNA crosslinks formed by the antitumor agent *cis*-$(NH_3)_2PtCl_2$ (Cisplatin). To date only mono(1-methylcytosine) complexes have been studied in detail [7], while with uracil and thymine only Pt complexes containing the *cis*-Pt(II) moiety bound through the N1 position have been structurally characterized [8].

We now report the crystal structure of the first example of a mono(1-methylthyminato) complex with Pt coordinated through N3, chloro-(1-methylthyminato-*N3*)-*cis*-diammineplatinum(II) monohydrate, *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)Cl \cdot H_2O$. We were interested in the structural details of this compound for comparison with related compounds containing bridging 1-methylthyminato ligands [9–11] as well as complexes of Pt(IV) with uracil and thymine nucleobases [12]:



Scheme 1.

Experimental

The compound was prepared from *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)_2$ and HCl as previously described [13]. The yield could be raised to 70% by the following modification: 2 mmol *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)_2 \cdot 2.5H_2O$ were dissolved in 20 ml 0.1 N HCl and the clear solution was kept for 10 min on a water bath at 90 °C and then for 2 d at 22 °C. The first crop, collected after 24 h, consisted of 310 mg of crystalline *cis*-$(NH_3)_2Pt(C_6H_7N_2O_2)Cl \cdot$

---

*Authors to whom correspondence should be addressed.

0020-1693/85/$3.30

H_2O. Later crops contained contaminations of *cis*-$(NH_3)_2PtCl_2$ and free ligand, which were separated by means of DMF and recrystallization from water as previously described [13].

A crystal of dimensions 0.5 X 0.3 X 0.2 mm was used for the X-ray measurements which were performed at room temperature with a PHILIPS PW-1100 single crystal diffractometer using monochromated Mo-Kα radiation (λ = 0.71069 Å). The compound crystallized in the triclinic space group $P\bar{1}$ with $Z = 2$. Cell dimensions were a = 6.911(2), b = 8.598(3), c = 11.464(4) Å, α = 100.13(3), β = 120.03(3), γ = 93.16(3)°, U = 572.37 Å^3, D_c = 2.447 g cm^{-3}, D_m = 2.44 g cm^{-3}. The cell parameters were obtained from 24 reflections (33° < 2θ < 43°). For the data collection a θ–2θ technique was used (θ_{max} = 23°). From the 1594 measured reflections, the set of 1577 reflections with $F_o > 2\sigma(F_o)$ was used for the structure determination. Lp and an empirical absorption correction (μ = 120.0 cm^{-1}) based on a program of Stuart and Walker [14] were applied. The position of the Pt atom was determined from a Patterson map, the other non-hydrogen atoms were located by subsequent ΔF-syntheses. H atoms were ignored at all stages of the calculations. Pt and Cl were refined with anisotropic, the other atoms with isotropic temperature factors; R = 0.048, R_w = 0.057; $w^{-1} = \sigma^2(F) + 0.0037\ F^2$. Atom parameters are listed in Table I. For Pt and Cl the equivalent isotropic temperature factors are given (calculated from the U_{ij} values by $U_{eq} = 1/3\Sigma_{ij}a_i{}^*a_j{}^*a_i{\cdot}a_j$). The highest peak in the final difference map was 1.6 eÅ^{-3} (1 Å away from Pt). Complex scattering factors for neutral atoms were taken from refs. 15 and 16. For the calculations the SHELX-program package was used [17]. As in similar structures containing 1-methylthymine ligands [1b, 9–11] the differentiation between the exocyclic oxygens O2 and O4 was not unambiguous due to the pseudo-twofold axis of the 1-MeT** ligand through N3 and C6. The assignment made in this work was based on the slightly better R value compared to O4/O2 and N1/C5 interchanged.

TABLE 1. Positional Parameters and Temperature Factors (Å^2).

Atom	x	y	z	U_{eq}
Pt1	0.2328(1)	0.2111(1)	0.0646(1)	0.019(1)
Cl1	0.6226(5)	0.2159(4)	0.1794(3)	0.038(3)
N10	0.2219(19)	0.1369(14)	−0.1145(12)	0.037(3)
N11	−0.1114(17)	0.2058(12)	−0.0401(11)	0.027(2)
N1	0.2106(15)	0.5053(10)	0.3934(9)	0.030(2)
C1′	0.1766(21)	0.6755(14)	0.4273(14)	0.043(3)
C2	0.2130(16)	0.4542(11)	0.2709(10)	0.021(2)
O2′	0.2031(12)	0.5393(9)	0.1937(8)	0.034(2)
N3	0.2379(17)	0.2889(12)	0.2388(11)	0.025(2)
C4	0.2469(15)	0.1891(10)	0.3210(10)	0.016(2)
O4′	0.2486(12)	0.0446(8)	0.2870(8)	0.034(2)
C5	0.2550(14)	0.2512(12)	0.4473(9)	0.016(2)
C5′	0.2663(21)	0.1431(15)	0.5345(14)	0.041(3)
C6	0.2317(17)	0.4074(12)	0.4775(11)	0.025(2)
O1	0.5609(19)	0.5898(13)	0.1459(11)	0.064(3)

Results

Figure 1 gives a view of the molecule, Table II lists selected interatomic distances and angles, and

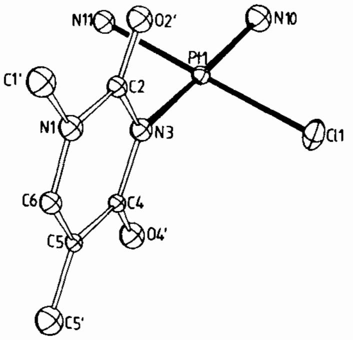


Fig. 1. Molecular structure of chloro-(1-methylthyminato)-*cis*-diammineplatinum(II).

TABLE II. Interatomic Distances (Å) and Angles (deg).

(a) Pt coordination sphere			
Pt1–Cl1	2.326(3)	Cl1–Pt1–N10	88.2(3)
Pt1–N10	2.002(11)	Cl1–Pt1–N11	178.9(3)
Pt1–N11	2.052(10)	Cl1–Pt1–N3	92.9(3)
Pt1–N3	1.973(10)	N10–Pt1–N11	90.7(4)
		N10–Pt1–N3	178.3(3)
		N11–Pt1–N3	88.1(4)
(b) Ligand geometry			
N1–C1′	1.509(15)	C1′–N1–C6	120.1(9)
N1–C2	1.405(13)	C1′–N1–C2	117.4(8)
C2–O2′	1.222(12)	C6–N1–C2	122.5(8)
C2–N3	1.447(13)	O2′–C2–N1	125.2(8)
N3–C4	1.363(15)	O2′–C2–N3	118.7(9)
C4–O4′	1.238(11)	N1–C2–N3	116.1(9)
C4–C5	1.424(13)	C2–N3–C4	120.7(9)
C5–C5′	1.458(18)	O4′–C4–N3	120.5(9)
C5–C6	1.365(13)	O4′–C4–C5	119.5(9)
C6–N1	1.348(14)	N3–C4–C5	119.9(9)
		C5′–C5–C4	119.2(9)
		C5′–C5–C6	121.5(9)
		C4–C5–C6	119.0(10)
		C5–C6–N1	121.5(10)

(continued on facing page)

**Abbreviations used: 1-MeT = deprotonated 1-methylthymine, 1-MeU = deprotonated 1-methyluracil, 1-MeC = 1-methylcytosine.

TABLE II *(continued)*

(c) Possible hydrogen bonding interactions^a

O2′–O1	2.82	C2–O2′–O1	121
N10–O4′^{1}	2.97	Pt1–N10–O4′^{1}	100
N11–O4′^{1}	2.91	Pt1–N11–O4′^{1}	100
N11–O2′^{2}	2.95	Pt1–N11–O2′^{2}	107
N10–O1^3	2.89	Pt1–N10–O1^3	105
O1–O1^3	3.08		

^{a}Symmetry transformations: $^1-x, -y, -z$; $^2-x, 1-y, -z$; $^3 1-x, 1-y, -z$.

conformational parameters are reported in Table III. Pt has a square-planar coordination geometry with angles close to 90°, and a normal distance of 2.326(3) Å to the Cl ligand. The Pt–N3(1-MeT) distance of 1.973(10) Å is the shortest so far observed for any Pt complex of uracil or thymine ligands. Not unexpectedly, it is shorter than in complexes containing a second metal bound through the O4 position, *e.g.* Pt [9, 10] or Ag [11a]. Values for the dinuclear head–tail complex are 2.014(9) and 2.064(8) Å [9] and for the dinuclear head–head complex 2.031(8) and 2.042(8) Å [10]. Surprisingly, however, this distance in the title compound is also shorter than in *cis*-$(NH_3)_2Pt(1\text{-}MeU)_2$ (2.034(8) and 2.050(8) Å) [18] and in complexes of unsubstituted uracil (2.04(1) Å) and thymine (2.036(5) Å) [8] with Pt binding occurring through N1.

TABLE III. Conformational Parameters.

(a) Deviation of Pt from least squares coordination plane^a
ΔPt −0.012 Å from Cl1, N10, N11, N3 (plane I)^b

(b) Deviations of exocyclic groups and of Pt from 1-MeT plane^a
ΔC1′ −0.085, ΔO2′ 0.039, ΔO4′ −0.131, ΔC5′ −0.030, ΔPt −0.011 Å from N1, C2, N3, C4, C5, C6 (plane II)^c

(c) Dihedral angle
plane I/plane II 76.5°

^{a}Equations of the planes refer to the *a b c* basis. $^b 0.98250x + 8.41669y - 3.66588z = 1.780$. $^c 5.88287x + 0.81912y - 0.34256z = 1.531$.

The coordination sphere of Pt is completed by two NH_3 groups in the *cis*-position to each other. The two bond lengths between Pt and NH_3 differ in the following way: Pt–NH_3 (*trans* to N3 of 1-MeT) is 2.002(11) Å, Pt–NH_3 (*trans* to Cl) is 2.052(10) Å. Whether this difference in Pt–NH_3 bond length reflects a difference in *trans*-influence of chloro *vs.* N(nucleobase), as suggested in a similar situation with *cis*-chlorodiammine(*N2*,*N2*-dimethyl-9-methylguanine)platinum(II) hexafluorophosphate [19], or a crystal packing effect, is unclear. It should be noted that, for example with *cis*-$(NH_3)_2Pt(1\text{-}MeC)Cl^+$ [7a], no such difference in Pt–NH_3 bond lengths is observed.

The 1-MeT ring is essentially planar as far as the endocyclic atoms are concerned. Of the exocyclic atoms, C1′ and O4′ deviate slightly, yet Pt is well within the plane. This fact may indeed account for the short Pt–N3(1-MeT) bond: with the bis(1-MeU) complex mentioned above, there is a marked deviation of Pt from the planes of the uracil rings [18]. Due to the large errors in the structure of neutral 1-methylthymine [20], the ligand geometry of the platinated 1-MeT ring cannot be compared with the free nucleobase. As far as a comparison with the dinuclear head–tail and head–head complexes of *cis*-Pt(II) is concerned, there is a trend to a shorter C4–O4′ bond in the mononuclear complex described here but, with one exception [9], the differences cannot be considered significant.

There is no intramolecular hydrogen bonding between the exocyclic oxygens of 1-MeT and the ammonia ligands as in related complexes of uracil and thymine with enPt(II) [8]. This is a consequence of the considerably larger dihedral angle between 1-MeT and the Pt coordination plane (76.5°) in the complex described here. However, extensive intermolecular hydrogen bonding exists between these groups (contacts 2.89–2.97 Å) as well as between the lattice water and O2′ and one of the two NH_3 groups.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft, the Technische Universität München, and the Fonds der Chemischen Industrie.

References

1 (a) B. Lippert, D. Neugebauer and G. Raudaschl, *Inorg. Chim. Acta, 78,* 161 (1983); (b) D. Neugebauer and B. Lippert, *Inorg. Chim. Acta, 67,* 151 (1982).
2 R. Beyerle and B. Lippert, *Inorg. Chim. Acta, 66,* 141 (1982).
3 (a) R. Faggiani, C. J. L. Lock and B. Lippert, *J. Am. Chem. Soc., 102,* 5418 (1980); (b) R. Faggiani, B. Lippert, C. J. L. Lock and R. A. Speranzini, *Inorg. Chem., 21,* 3216 (1982).
4 (a) R. Faggiani, B. Lippert, C. J. L. Lock and R. Pfab, *Inorg. Chem., 20,* 2381 (1981). (b) B. Lippert, R. Pfab and D. Neugebauer, *Inorg. Chim. Acta, 37,* L495 (1979).
5 (a) U. Thewalt, D. Neugebauer and B. Lippert, *Inorg. Chem., 23,* 1713 (1984); (b) B. Lippert, U. Thewalt, H. Schöllhorn, D. M. L. Goodgame and R. W. Rollins, *Inorg. Chem., 23,* 2807 (1984).
6 B. Lippert, H. Schöllhorn and U. Thewalt, *Z. Naturforsch., Teil B:, 38,* 1441 (1983).

7 (a) B. Lippert, C. J. L. Lock and R. A. Speranzini, *Inorg. Chem., 20*, 335 (1981); (b) J. P. Britten, B. Lippert, C. J. L. Lock and P. Pilon, *Inorg. Chem., 21*, 1936 (1982).

8 R. Faggiani, B. Lippert and C. J. L. Lock, *Inorg. Chem., 19*, 295 (1980).

9 C. J. L. Lock, H. J. Peresie, B. Rosenberg and G. Turner, *J. Am. Chem. Soc., 100*, 3371 (1978).

10 H. Schöllhorn, U. Thewalt and B. Lippert, *Inorg. Chim. Acta, 93*, 19 (1984).

11 (a) B. Lippert and D. Neugebauer, *Inorg. Chim. Acta, 46*, 171 (1980); (b) B. Lippert and U. Schubert, *Inorg. Chim. Acta, 56*, 15 (1981).

12 G. Müller, J. Riede, R. Beyerle-Pfnür and B. Lippert, *J. Am. Chem. Soc., 106*, 7999 (1984).

13 B. Lippert, *Inorg. Chim. Acta, 55*, 5 (1981).

14 N. Walker and D. Stewart, *Acta Crystallogr., Sect. A:, 39*, 158 (1983).

15 D. T. Cromer and J. B. Mann, *Acta Crystallogr., Sect. A:, 24*, 321 (1968).

16 D. T. Cromer and D. Liberman, *J. Chem. Phys., 53*, 1891 (1970).

17 G. M. Sheldrick, 'SHELX-76', Program System, University of Göttingen, Göttingen, 1976.

18 D. Neugebauer and B. Lippert, *J. Am. Chem. Soc., 104*, 6596 (1982).

19 J. D. Orbell, C. Solorzano, L. G. Marzilli and T. J. Kistenmacher, *Inorg. Chem., 21*, 3806 (1982).

20 K. Hoogsteen, *Acta Crystallogr., 16*, 28 (1963).